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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/582,385	08/15/2007	Marco Antonio Santini	4705-0121PUS1	2824

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EXAMINER	
MERCIER, MELISSA S	

ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
03/19/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/582,385	SANTINI ET AL.	
	Examiner	Art Unit	
	MELISSA S. MERCIER	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50-66* is/are pending in the application.

4a) Of the above claim(s) *56-59 and 61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50-55,60 and 62-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6-9-06, 9-15-06, 11-27-07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Change of Examiner

The examiner assigned to the instant application has changed. The new examiner is Melissa Mercier. Contact information is provided at the end of this Office Action.

Summary

Receipt of Applicants Remarks and Amended Claims filed on August 19, 2008 is acknowledged. Claims 1-49 have been cancelled by Applicant. New Claims 50-66 have been submitted.

Information Disclosure Statement

Receipt of the Information Disclosure Statements filed on June 9, 2006, September 15, 2006, and November 27, 2007 is acknowledged. Signed copies are attached to this office action. It appears that the IDS's filed on June 9, 2006 and November 27, 2007 is duplicates.

Election/Restrictions

Applicant's election with traverse of Group IV, claims 1-2, and 4-6, and elected compound I, docetaxel, and ethanol as the solvent, as originally filed in the reply filed on July 30, 2008 is acknowledged. The traversal is on the ground(s) that the restriction requirement is incorrect and should have been a species election. This is not found

persuasive because the case is filed as a 371 and subject to Lack of Unity. The special technical feature has been found in the prior art, as cited in the office action. (see page 4), thereby breaking unity of invention and allowing for restriction between inventions.

The requirement is still deemed proper and is therefore made FINAL.

Applicant has cancelled all claims and presented new claims 50-66. Applicant has states that claim 51-59 read on the elected grouping and claims 50 and 60-66 are generic. Applicant has elected compound (I) and ethanol as a solvent. Claims 56-59 and 61 have been withdrawn from consideration as not reading on the elected compound (I), but rather compounds (II) and (III) and a combination of solvents not elected.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 50-55, 60, and 62-66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear if Applicant is claiming just the excipient have a pH in the range of 3.0-6.5 or either the vehicle or excipient. Clarification is requested. The examiner has interpreted the pH limitation to only apply to the excipient.

Claims 64-66 recite the limitation "the acid" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. Claim 50, from which the claim depends

does not comprise "an acid". It is unclear is Applicant is attempting to define the solvent and the antioxidant to be "an acid" and use the terms interchangeably.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 50 and 60, 62-63 are rejected under 35 U.S.C. 102(b) as being anticipated by Bastart. (US Patent 5,698,582)

Bastart discloses compositions containing taxane derivatives, consisting of solutions of such derivatives in a surfactant. The solutions are used to prepare perfusion solutions (abstract).

Taxol and Taxotere are disclosed as known derivatives encompassed by the general formula disclosed in column 1 (column 2, lines 1-3). Taxol and Taxotere are paclitaxel and docetaxel, respectively. The compounds can be dissolved in a surfactant, such as polysorbate (column 2, lines 53-56). Polysorbate 80 is disclosed (Examples). The stock solution may be prepared by dissolving the active principle in ethanol, and then gradually add the surfactant. Solutions containing 10-100mg/ml if active can be prepared. The ethanol is then completely or almost completely removed (column 3, lines 5-10). While the reference requires the use of a surfactant, it is noted that Applicant has employed comprising language allowing for such an inclusion.

Example 8 discloses filtering solutions through a 0.2um filter, prior to final dilution.

Paclitaxel and Docetaxel generically are known to be anhydrous compounds; therefore, the generic recitation would read on the limitation "having a water content less than 1.0% w/w.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 50, 60, and 62-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chi et al. (US 2003/0158249).

Chi discloses the use of anhydrous docetaxel, or a hydrate thereof, in the manufacture of a medicament (abstract). Since anhydrous means no water is present, and then the disclosure of anhydrous docetaxel meets the limitation of "having a water content of lower than 1.0% w/w. Pharmaceutical compositions containing docetaxel can be formulated with a pharmaceutically acceptable carrier or diluents suitable for parenteral administration (paragraph 0014). Suitable sterile non-aqueous solutions and suspensions include vegetable oils or in injectable organic esters. It is particularly preferred that solutions suitable for administration by infusion have a pH similar to that of the blood and are isotonic (paragraph 0015). Pharmaceutical compositions may further comprise a surfactant, such as polysorbates (paragraph 0017). A solution suitable for intravenous injection contains from 38-42mg/mL (paragraph 0021).

Chi does not disclose adding the docetaxel at a temperature of 20-40C or filtering the solution. However, it is noted that 20-40C is typical room temperature; therefore, since the art does not disclose a heating or cooling parameter, it is the position of the examiner that standard laboratory temperature would be employed. Furthermore, filtering is a common and well known practice for inject able pharmaceutical

formulations. Therefore, the skilled artisan would have known to filter the formulation of Chi in order to remove larger particles from the solution prior to administration.

Claims 51-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bastart (US Patent 5,698,582) in view of Sharma et al. (US 2004/0116720).

The teachings of Bastart are discussed above and applied in the same manner.

Bastart additionally discloses in Example 1, an azeotropic distillation in which taxotere (docetaxel) dissolved in ethanol and polysorbates 80. The ethanol is evaporated off in a rotary evaporator at 30C at a pressure of 15mmHg for 2hours.

Bastart does not disclose the starting active agent as a hydrate.

Sharma disclose the process for the preparation of paclitaxel trihydrate and docetaxel trihydrate (title). The crystallization is also preformed in the presence of ascorbic acid (paragraph 0003). The hydrated forms of the active agents are disclosed as having markedly superior stabile in comparison to the anhydrous product (paragraph 0004).

It would have been obvious to one of ordinary skill in the art at the time the inventing was made to have used the trihydrate forms of the active agents as disclosed by Sharma since Bastart discloses stable anhydrous solutions of docetaxel and Sharma discloses the crystals of the hydrated docetaxel are more stable. Therefore, it would have been obvious to have used the hydrated docetaxel in the place of the anhydrous docetaxel in the method disclosed in Example 1, which discloses an azeotropic distillation of the active agent.

Claims 64-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bastart (US Patent 5,698,582) in view of Zeldis et al. (US Patent 7,435,726).

The teachings of Bastart are discussed above and applied in the same manner.

Bastart does not disclose the use of an antioxidant in his formulation

Zeldis discloses injectable solutions of anticancer drugs, include taxotere and taxi. Zeldis discloses the addition of antioxidants such as ascorbic acid to the injectable formulations in order to reduce the rate by which the active ingredient will decompose (column 21, lines 4-10).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have incorporated an antioxidant into the vehicle in order to reduce the rate of drug decomposition as disclosed by the art of Zeldis.

Applicant is reminded that where the general conditions of the claims are met, burden is shifted to applicant to provide a patentable distinction. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. See In re Aller, 220 F.2d 454 105 USPQ 233,235 (CCPA 1955).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA S. MERCIER whose telephone number is (571)272-9039. The examiner can normally be reached on 8:00am-4:30pm Mon through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Melissa S Mercier/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615